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Multicenter Antimicrobial Susceptibility Survey of Gram-Negative Bacteria Isolated from Patients with Community-Acquired Infections in the People's Republic of China

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A survey of 2,099 gram-negative bacilli from community infections at seven centers in the People's Republic of China is reported. The rates of resistance of 1,615 isolates of the family *Enterobacteriaceae* were as follows: 40.8% for ciprofloxacin, 32.2% for gentamicin, 0% for imipenem or ertapenem, and 14.7% for cefotaxime. The rates of extended-spectrum β-lactamase production were 16% for *Escherichia coli* and 17% for *Klebsiella*.

In the People's Republic of China (PRC), the widespread use of antibiotics had led to very high levels of antimicrobial resistance among bacterial isolates from patients with nosocomial infections (3, 11, 13). However, there has been no comprehensive study of the susceptibilities of gram-negative bacilli (GNB) from the community in the PRC. The high prevalence of extended-spectrum β-lactamase (ESBL)-producing GNB in hospitals (3, 12, 13) suggests that they may be common in the community. Because of the broad spectrum of activity of ertapenem and its potential for the treatment of community-acquired infections (CAIs), it was included with 11 other antibiotics in the first multicenter antimicrobial surveillance study of CAI in the PRC. Gram-negative bacilli isolated from outpatients or patients in the community with clinically significant infections (within 48 h of admission to hospital) in seven geographical areas in the PRC (Beijing, Guangzhou, Hong Kong, Hunan, Shanghai, Wuhan, and Zhejiang) were studied by using 23 collecting laboratories or institutions during 2002 and 2003.

A total of 2,099 nonduplicate clinical isolates of gram-negative bacteria were identified by using the MAST-ID system (Mast Diagnostics, Bootle, United Kingdom) and API 20E/NE strips (bioMérieux, Marcy l'Etoile, France) in both Guangzhou and Hong Kong. Bacterial isolates were collected from urine (38%), tracheal aspirates or sputum (21%), soft tissue (17%), blood (7%), bile (4%), and unspecified sites (13%).

The MICs of the 12 agents tested (Table 1) for all isolates were determined by the CLSI (formerly the NCCLS) agar dilution methodology (9) in the Hong Kong center. ESBL production was confirmed by using ceftazidime (30 μg) and cefotaxime (30 μg) disks with and without clavulanic acid (10 μg) for isolates of the family *Enterobacteriaceae* with MICs ≥1 μg/ml to ceftazidime or cefotaxime, with a zone diameter difference of ≥5 mm indicating phenotypic confirmation of ESBL production (9).

Table 1 shows the activities of ertapenem and the 11 other antibiotics against the study isolates. The susceptibilities of the *Enterobacteriaceae* to carbapenems (100%), some broad-spectrum and newer, "fourth-generation" (cefepime) cephalosporins, and amikacin (>90%) were high; but cefotaxime and cefoperazone showed reduced activities (susceptibility rates, 85% and 83%, respectively). High rates of resistance to ciprofloxacin (41%) and gentamicin (32%) were found among the *Enterobacteriaceae*. No isolate of the *Enterobacteriaceae* was resistant to ertapenem or imipenem. Ertapenem was the most active agent against all isolates of the *Enterobacteriaceae*, with an MIC at which 90% of isolates are inhibited (MIC_{90}) of 0.06 μg/ml, followed by imipenem, with an MIC_{90} of 0.5 μg/ml.

Ertapenem demonstrated greater antimicrobial activity than imipenem against the *Enterobacteriaceae*, with the ertapenem MIC_{90} being eight times lower than that of imipenem. These findings are similar to those from European, Australian, and American studies (4, 6, 7). However, ertapenem was less active against *Acinetobacter* spp. and *Pseudomonas* spp., with resistance rates of 52% and 81%, respectively, which were higher than those from a previous report from Europe and Australia (7). Therefore, imipenem would be a better choice than ertapenem for the treatment of CAIs caused by these two organisms, particularly for those cause by *Acinetobacter* spp. (susceptibility rate, 97%). The percentages of gentamicin-resistant *Escherichia coli* and *Klebsiella* spp. were 40% and 19%, respectively, and were higher than those found in 20 European countries (4.3% and 9.1%, respectively) (10). The rate of ciprofloxacin resistance in *E. coli* (50%) was higher than that found in all Asia-Pacific countries included in a SENTRY study (1 to 30%) (1). Such a high percentage of ciprofloxacin resistance is probably driven by the spread of quinolone-resistant nosocomial *E. coli* isolates into the community in the PRC (3, 11, 13) and the strong and ubiquitous selection pressure caused by the over-the-counter purchase and community use of fluoroquinolones in the PRC. Isolates from Hong Kong had the lowest

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TABLE 1. MIC profiles of 12 antibiotics against 2,099 gram-negative bacteria isolated from patients with community acquired infections in the PRC (2002 and 2003)[a]

Organism (no. tested) and antibiotic	MIC (μg/ml)			% Resistant
	50%	90%	Range	
All isolates of the *Enterobacteriaceae* (n = 1,615)				
Ertapenem	≤0.03	0.06	≤0.03–2	0
Imipenem	0.12	0.5	≤0.03–4	0
Cefotaxime	0.06	32	≤0.06–≥64	14.7
Ceftazidime	0.25	4	≤0.06–≥64	5.9
Cefepime	0.12	8	≤0.06–≥64	8.3
Cefoperazone	1	≥64	≤0.06–≥64	16.5
Cefoperazone-sulbactam	0.5	16	≤0.06–≥64	5.5
Amoxicillin-clavulanate	8	≥64	≤0.06–≥64	33.0
Piperacillin-tazobactam	4	16	≤0.06–≥128	9.5
Ciprofloxacin	0.25	≥32	≤0.03–≥32	40.8
Gentamicin	1	≥64	≤0.06–≥64	32.2
Amikacin	2	4	≤0.06–≥64	4.2
E. coli (n = 953)				
Ertapenem	≤0.03	0.06	≤0.03–2	0
Imipenem	0.12	0.12	≤0.03–4	0
Cefotaxime	0.12	32	≤0.06–≥64	14.4
Ceftazidime	0.25	2	≤0.06–≥64	2.7
Cefepime	0.12	8	≤0.06–≥64	8.0
Cefoperazone	1	≥64	≤0.06–≥64	17.3
Cefoperazone-sulbactam	1	16	≤0.06–≥64	4.6
Amoxicillin-clavulanate	8	16	≤0.06–≥64	29.1
Piperacillin-tazobactam	4	16	≤0.06–≥128	7.1
Ciprofloxacin	2	≥32	≤0.03–≥32	50.6
Gentamicin	1	≥64	≤0.06–≥64	39.4
Amikacin	2	4	≤0.06–≥64	2.4
Klebsiella spp. (n = 357)				
Ertapenem	≤0.03	0.12	≤0.03–1	0
Imipenem	0.12	0.25	0.06–2	0
Cefotaxime	≤0.06	32	≤0.06–≥64	15.4
Ceftazidime	0.25	8	≤0.06–≥64	8.1
Cefepime	0.12	8	≤0.06–≥64	8.1
Cefoperazone	0.5	≥64	≤0.06–≥64	16.3
Cefoperazone-sulbactam	0.25	16	≤0.06–≥64	6.7
Amoxicillin-clavulanate	2	32	0.5–≥64	20.2
Piperacillin-tazobactam	4	32	05–≥128	13.2
Ciprofloxacin	≤0.03	≥32	≤0.03–≥32	25.2
Gentamicin	0.5	≥64	≤0.06–≥64	18.8
Amikacin	1	8	0.25–≥64	7.3
Enterobacter spp., *Serratia* spp., and *Citrobacter* spp. (n = 175)				
Ertapenem	≤0.03	0.25	≤0.03–2	0
Imipenem	0.25	0.5	≤0.03–2	0
Cefotaxime	0.25	≥64	≤0.06–≥64	25.1
Ceftazidime	0.5	≥64	≤0.06–≥64	20.0
Cefepime	0.12	32	≤0.06–≥64	16.6
Cefoperazone	1	≥64	≤0.06–≥64	22.3
Cefoperazone-sulbactam	0.5	32	≤0.06–≥64	12.0
Amoxicillin-clavulanate	≥64	≥64	0.5–≥64	88.0
Piperacillin-tazobactam	4	64	0.5–≥128	21.7
Ciprofloxacin	0.06	16	≤0.03–≥32	22.9
Gentamicin	0.5	≥64	0.12–≥64	24.0
Amikacin	2	32	0.5–≥64	10.3
Proteus mirabilis (n = 76)				
Ertapenem	≤0.03	≤0.03	≤0.03–≤0.03	0
Imipenem	1	2	≤0.03–4	0
Cefotaxime	≤0.06	≤0.06	≤0.06–0.12	0
Ceftazidime	≤0.06	≤0.06	≤0.06–0.25	0
Cefepime	≤0.06	0.12	≤0.06–0.25	0
Cefoperazone	1	2	0.12–16	0
Cefoperazone-sulbactam	0.5	1	0.12–2	0
Amoxicillin-clavulanate	1	4	0.25–8	0
Piperacillin-tazobactam	0.5	1	0.25–8	0
Ciprofloxacin	0.06	8	≤0.03–≥32	36.8
Gentamicin	0.5	≥64	0.25–≥64	29.0
Amikacin	2	4	1–8	0
Indole-positive *Proteus* spp. (n = 47)				
Ertapenem	≤0.03	≤0.03	≤0.03–0.5	0

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TABLE 1—*Continued*

Organism (no. tested) and antibiotic	MIC (μg/ml)			% Resistant
	50%	90%	Range	
Imipenem	2	4	0.25–4	0
Cefotaxime	≤0.06	2	≤0.06–32	4.3
Ceftazidime	0.12	2	≤0.06–64	8.5
Cefepime	≤0.06	1	≤0.06–8	0
Cefoperazone	2	16	0.5–≥64	8.5
Cefoperazone-sulbactam	1	4	0.25–8	0
Amoxicillin-clavulanate	≥64	≥64	1–≥64	66.0
Piperacillin-tazobactam	1	8	0.25–32	2.1
Ciprofloxacin	1	32	≤0.03–≥32	40.4
Gentamicin	0.5	≥64	0.12–≥64	27.7
Amikacin	2	4	0.5–≥64	2.1
Pseudomonas aeruginosa (*n* = 272)				
Ertapenem	8	32	≤0.03–≥32	81.6
Imipenem	2	8	≤0.03–≥32	11.0
Cefotaxime	32	≥64	≤0.06–≥64	85.7
Ceftazidime	2	32	0.12–≥64	17.7
Cefepime	4	32	≤0.06–≥64	34.3
Cefoperazone	8	≥64	0.12–≥64	24.3
Cefoperazone-sulbactam	8	32	0.12–≥64	16.5
Amoxicillin-clavulanate	≥64	≥64	2–≥64	97.4
Piperacillin-tazobactam	8	64	0.25–≥128	8.1
Ciprofloxacin	0.25	4	≤0.03–≥32	16.5
Gentamicin	4	≥64	0.12–≥64	27.9
Amikacin	8	32	≤0.06–≥64	13.2
Other nonfermenters (*n* = 31)				
Ertapenem	8	32	≤0.03–≥32	61.3
Imipenem	2	32	≤0.03–≥32	21.8
Cefotaxime	32	≥64	≤0.06–≥64	80.7
Ceftazidime	4	≥64	0.12–≥64	22.6
Cefepime	16	≥64	≤0.06–≥64	67.7
Cefoperazone	16	64	0.12–≥64	45.2
Cefoperazone-sulbactam	8	64	0.25–≥64	22.6
Amoxicillin-clavulanate	64	≥64	1–≥64	71.0
Piperacillin-tazobactam	8	64	0.5–>128	6.5
Ciprofloxacin	1	8	≤0.03–32	35.5
Gentamicin	64	≥64	0.25–≥64	58.1
Amikacin	16	≥64	≤0.06–≥64	48.4
Stenotrophomonas maltophilia (*n* = 29)				
Ertapenem	≥32	≥32	2–≥32	96.6
Imipenem	≥32	≥32	8–≥32	100
Cefotaxime	64	≥64	2–≥64	89.7
Ceftazidime	16	≥64	1–≥64	62.1
Cefepime	32	64	4–≥64	86.2
Cefoperazone	16	64	2–≥64	31.0
Cefoperazone-sulbactam	8	32	2–≥64	17.0
Amoxicillin-clavulanate	≥64	≥64	16–≥64	100
Piperacillin-tazobactam	32	≥128	8–≥128	24.1
Ciprofloxacin	2	16	0.5–32	69.0
Gentamicin	≥64	≥64	4–≥64	93.1
Amikacin	≥64	≥64	16–≥64	96.6
Acinetobacter spp. (*n* = 120)				
Ertapenem	4	16	≤0.03–≥32	51.7
Imipenem	0.25	2	≤0.03–≥16	3.3
Cefotaxime	8	≥64	≤0.06–≥64	50.0
Ceftazidime	4	≥64	0.12–≥64	25.0
Cefepime	4	≥64	≤0.06–≥64	29.2
Cefoperazone	32	64	0.25–≥64	71.7
Cefoperazone-sulbactam	1	32	≤0.06–≥64	12.5
Amoxicillin-clavulanate	16	≥64	≤0.06–≥64	50.8
Piperacillin-tazobactam	8	64	≤0.06–≥128	29.2
Ciprofloxacin	0.25	≥32	≤0.03–≥32	35.0
Gentamicin	1	≥64	≤0.06–≥64	22.5
Amikacin	2	≥64	0.25–≥64	23.3
ESBL-producing *E. coli* (*n* = 151)				
Ertapenem	≤0.03	0.12	≤0.03–1	0
Imipenem	0.12	0.12	0.03–0.25	0
Cefotaxime	32	64	1–≥64	86.1
Ceftazidime	2	16	0.25–≥64	13.3

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TABLE 1—*Continued*

Organism (no. tested) and antibiotic	MIC (μg/ml)			% Resistant
	50%	90%	Range	
Cefepime	8	64	0.5–≥64	47.7
Cefoperazone	≥64	≥64	2–≥64	96.7
Cefoperazone-sulbactam	16	32	1–≥64	25.2
Amoxicillin-clavulanate	16	32	4–≥64	53.6
Piperacillin-tazobactam	8	32	1–128	13.9
Ciprofloxacin	32	≥32	≤0.03–≥32	76.8
Gentamicin	32	≥64	0.12–≥64	64.9
Amikacin	2	16	0.5–≥64	7.3
ESBL-producing *Klebsiella* spp. (n = 59)				
Ertapenem	0.06	0.25	≤0.03–0.5	0
Imipenem	0.12	0.25	0.06–2	0
Cefotaxime	32	≥64	0.5–≥64	81.0
Ceftazidime	8	≥64	0.5–≥64	44.8
Cefepime	8	64	0.12–≥64	43.1
Cefoperazone	≥64	≥64	1–≥64	79.3
Cefoperazone-sulbactam	16	64	0.25–≥64	32.8
Amoxicillin-clavulanate	16	≥64	2–≥64	62.1
Piperacillin-tazobactam	16	64	1–128	43.1
Ciprofloxacin	8	≥32	≤0.03–≥32	67.2
Gentamicin	32	≥64	0.25–≥64	53.5
Amikacin	2	≥64	0.5–≥64	27.6
ESBL-producing *Enterobacter* spp., *Serratia* spp., and *Citrobacter* spp. (n = 43)				
Ertapenem	0.25	2	≤0.03–2	0
Imipenem	0.25	0.5	0.06–1	0
Cefotaxime	64	≥64	4–≥64	86.1
Ceftazidime	64	≥64	1–≥64	62.8
Cefepime	16	≥64	1–≥64	62.8
Cefoperazone	≥64	≥64	2–≥64	83.7
Cefoperazone-sulbactam	16	≥64	1–≥64	44.2
Amoxicillin-clavulanate	≥64	≥64	8–≥64	93.0
Piperacillin-tazobactam	32	≥128	8–≥128	74.4
Ciprofloxacin	2	≥32	≤0.03–≥32	55.8
Gentamicin	≥64	≥64	0.25–≥64	72.1
Amikacin	8	≥64	1–≥64	34.9

[a] The MIC profiles of 12 antibiotics against *Aeromonas* spp. (n = 14) and other organisms (n = 18) are not included here.

rates of resistance to all the antimicrobials tested, except that 17% of the *Klebsiella* sp. isolates were resistant to ceftazidime; *E. coli* isolates from Beijing and Shanghai had the highest rates of ciprofloxacin resistance (67% and 63%, respectively). *Acinetobacter* sp. isolates from these two centers also had the highest rates of resistance to β-lactams. These differences are probably due to the proliferation of individual strains and differences in prescription policies in the centers.

The prevalence of ESBL production in *E. coli* was 16% and was higher than that in all Asia-Pacific countries included in the SENTRY study, in which the prevalence of ESBL production in *E. coli* ranges from 0.5% to 11.3% (5). In contrast, the prevalence of ESBL production in *Klebsiella* spp. was 17% and was comparable to that among isolates from other Asia-Pacific countries (5). ESBL-producing *E. coli* and *Klebsiella* spp. showed coresistance to ciprofloxacin (resistance rates, 76.8% and 67.2%, respectively) and gentamicin (resistance rates, 64.9% and 53.5%, respectively) (Table 1), which is similar to the findings reported in the SENTRY study (5). The prevalence of ESBL production found among community isolates in our study was lower than that detected among nosocomial isolates (40%) in the PRC (3, 11, 13), and the susceptibility patterns of individual antibiotic-species combinations for isolates from both the community and hospitals were quite similar (3). A number of studies have shown that ESBL producers are common among nosocomial isolates in the PRC, particularly CTX-M types, with CTX-M-14 being dominant (2, 8); the genes for CTX-M ESBLs may well have spread into community-associated isolates of the family *Enterobacteriaceae*. The high levels of resistance found in the gram-negative bacilli in CAIs in the PRC make the choice of empirical antibiotic regimens difficult. Carbapenems such as imipenem and ertapenem are therefore the best choice for the treatment of CAIs in the PRC. The high levels of ESBL-producing isolates of the family *Enterobacteriaceae* found in this study warrant further genetic characterization of the isolates.

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